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POSTER PRESENTATION

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P10. Concomitant gemcitabine therapy negatively affects DC vaccine-induced CD8⁺ T cell and B cell responses but improves clinical efficacy in a murine pancreatic carcinoma model

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Background

Multiple studies have shown that dendritic cell (DC)-based vaccines can induce antitumor immunity. Previously, we reported that gemcitabine enhances the efficacy of DC vaccination in a mouse model of pancreatic carcinoma. The present study aimed at investigating the influence of gemcitabine on vaccine-induced anti-tumoral immune responses in a syngeneic pancreatic cancer model.

Material and methods

Subcutaneous or orthotopic pancreatic tumours were induced in C57BL/6 mice using Panc02 cells expressing the model antigen OVA (PancOVA). Bone marrow-derived DC were loaded with soluble OVA protein (OVA-DC). Animals received gemcitabine twice weekly. OVA-specific CD8⁺ T cells and antibody titers were monitored by FACS analysis and ELISA, respectively.

Results

Gemcitabine enhanced clinical efficacy of the OVA-DC vaccine. Interestingly, gemcitabine significantly suppressed the vaccine-induced frequency of antigen-specific CD8⁺ T cells and antibody titers. DC migration to draining lymph nodes and antigen cross-presentation were unaffected. Despite reduced numbers of tumour-reactive T cells in peripheral blood, *in vivo* cytotoxicity assays revealed that CTL-mediated killing was preserved. *In vitro* assays revealed sensitization of tumour cells to CTL-mediated lysis by gemcitabine. In addition, gemcitabine facilitated recruitment of CD8⁺ T cells into tumors in

DC-vaccinated mice. T and B cell suppression by gemcitabine could be avoided by starting chemotherapy after two cycles of DC vaccination.

Conclusions

Gemcitabine enhances therapeutic efficacy of DC vaccination despite its negative influence on vaccine-induced T cell proliferation. Quantitative analysis of tumour-reactive T cells in peripheral blood may thus not predict vaccination success in the setting of concomitant chemotherapy.

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